

Claims

1) Use of a CCT complex or part thereof for identifying a binding member capable of occupying a substrate binding site on the CCT complex or part thereof wherein the binding member inhibits the binding of the CCT substrate and the CCT complex.

2) Use according to claim 1 wherein the binding member is an antibody.

3) Use according to claim 1 wherein the binding member is a peptide or a peptide fragment.

4) Use according to claim 3 wherein the peptide or peptide fragment is greater than 5 amino acids in length.

5) Use according to claim 4 wherein the peptide or peptide fragment is from 5 to 40 amino acids in length.

6) Use according to any one of claims 3 to 5 wherein the peptide or peptide fragment is derived from a CCT substrate.

7) Use according to claim 6 wherein the substrate is selected from the group consisting of actin, tubulin or cyclin.

8) Use according to claim 7 wherein the substrate is actin.

9) Use according to any one of claims 3 to 8 wherein the peptide or peptide fragments comprises any one of the sequences shown in Figure 10.

10) Use according to any one of claims 3 to 9 wherein the peptide or peptide fragment comprises the amino acid sequence GRPRH.

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Sub A1
11) A method of identifying a binding member capable of occupying a substrate binding site on a CCT apical domain; comprising the steps of
contacting a candidate binding member with said CCT apical domain; and

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determining binding between said candidate binding member and the CCT apical domain.

12) A method according to claim 11 wherein the binding member is a peptide or peptide fragment.

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13) A method according to claim 11 or claim 12 wherein the candidate binding member is a peptide or peptide fragment having an amino acid sequence corresponding to the amino acid sequence of a CCT apical domain.

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14) A method according to claim 13 wherein the CCT substrate is actin.

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15) A method according to claim 14 wherein the CCT substrate is tubulin.

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Sub A2
16) A method according to any one of claims 12 to 14 wherein the peptide or peptide fragment comprises any one of the sequences as shown in Fig. 10.

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17) A method according to any one of claim 11 to 16 further comprising the step of immobilising the candidate binding member on a solid phase prior to contacting with the CCT apical domain.

18) A method according to any one of claims 11 to 17 further comprising the step of modifying the candidate binding member to improve its binding with the CCT apical domain.

19) A method according to any one of claim 11 to 18 wherein binding between the candidate binding member and the CCT apical domain is determined by a competitive assay.

20) A binding member capable of occupying a CCT substrate binding site, comprising of an amino acid sequence of 5 to 40 amino acids derived from a CCT substrate.

21) A binding member according to claim 20 wherein the CCT substrate is selected from the group consisting of actin, tubulin or cyclin.

22) A binding member according to claim 21 wherein the CCT substrate is actin.

23) A binding member according to claim 22 comprising any one of the amino acid sequences as shown in Fig. 10.

24) A binding member according to claim 23 comprising the amino acid sequence GRPRH

25) A binding member according to any one of claims 20 to 24 for use in binding to a CCT complex such that it blocks a substrate binding site on said CCT complex thereby effecting the biological activity of the CCT complex.

26) A binding member according to any one of claims 20 to 25 linked to a coupling partner.

27) A binding member according to claim 26 wherein the coupling partner is a second peptide and the binding member and the second peptide form a fusion protein.

5 28) A binding member according to any one of claims 20 to claim 27 for use in medical treatment.

Sub A5
10 29) Use of a binding member according to any one of claims 20 to 27 in the preparation of a medicament for the treatment of cancer cells wherein the medicament is administered to said cells to effect the biological activity of a CCT complex within the cell.

15 30) Use according to claim 39 wherein the medicament further comprises a cancer drug.

20 31) A method for screening for mimetics of binding members according to any one of claims 20 to 27 comprising exposing said binding members and a candidate mimetic to a CCT substrate binding site or active portion thereof, so that the candidate mimetic and the binding member compete to bind to the CCT substrate binding site; and detecting the extent of binding of the candidate mimetic or the binding member to the CCT substrate
25 binding site.

32) A method according to claim 31 further comprising screening the candidate mimetics for biological activity.

30 33) A method according to claim 32 wherein the biological activity is the inhibition of cytoskeletal assembly.

35 34) A method according to claim 32 wherein the biological activity is CCT complex dis-assembly.

35) A method according to any one of claims 27 to 34 wherein the binding member or the candidate mimetic is immobilised on a solid support.

36) A method according to any one of claims 31 to 35 wherein the extent of binding of the candidate mimetic is detected by labelling the CCT substrate binding site complex or active portion thereof or by using a labelled antibody capable of binding to the CCT substrate binding domain.

37) A method according to any one of claims 31 to 36 wherein the CCT substrate binding site comprises the sequence corresponding to residues D219 to N394 of CCTδ.

38) A pharmaceutical composition comprising a binding member according to any one of claim 20 to 28 in combination with a pharmaceutically acceptable carrier.

39) A CCT apical domain having at least 80% homology with the amino acid sequence of D219 to N394 of CCTδ.

40) A nucleic acid molecule encoding the polypeptide according to claim 39.

41) A vector comprising the nucleic acid according to claim 40.

42) A host cell comprising the vector according to claim 41 or the nucleic acid according to claim 40.